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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/281,349	10/25/2002	Stanley T. Crooke	~~ISIS0002-105/130528~~	4628

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EXAMINER	
MCGARRY, SEAN	
ART UNIT	**PAPER NUMBER**
1635	
MAIL DATE	**DELIVERY MODE**
12/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/281,349	CROOKE, STANLEY T.	
	Examiner	Art Unit	
	/Sean R. McGarry/	1635	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43,44,94-104 and 135-189* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43, 44, 94-104, and 135-189* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/19/07 has been entered.

Upon entry of the amendments filed 9/17/07, claims 43, 44, 94-104, 135-158, and new claims 159-189 are pending.

The terminal disclaimer filed 9/19/07 has been approved and entered.

Claims 43, 44, 94-104, and 135-158 **were** rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 6,107,094. the filing of a TD on 9/19/07 obviates this rejection.

Claims 43, 44, 94-98, 136-142, and 146-158 **were** rejected under 35 U.S.C. 103(a) as being unpatentable over Goodchild [US 6,573,072]. This rejection has been withdrawn in view of applicants amendments to the claims and also withdrawn in favor of the new rejection below.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Claim Objections

Claims 146 and160 objected to because of the following informalities: In claim 146, line 7, "comprprises" appears to be a typographical error. In claim 160 "claim159" should have a spece between "claim" and "159". Appropriate correction is required.

Claim Rejections - 35 USC § 103

Claims 43, 44, 94-98, 136-142, and 146-158 rejected under 35 U.S.C. 103(a) as being unpatentable over Goodchild [US Patent 6,087,484].

The claimed invention is as clearly set forth in the claims; no interpretation is required to apply the art.

Goodchild teaches facilitator oligonucleotides that enhance the catalytic properties of ribozymes. The facilitator oligonucleotides are taught to be from 5 to 50 and 10-15 nucleotides in length(see columns 1 and 3 and claim 6, for example). It is taught at column2-3 that the oligonucleotides can be RNA or DNA or a combination thereof. It is taught that the oligonucleotides can include modifications to the base,

sugar and backbone. It is taught that the modifications provide nuclease resistance and it is asserted that this is desirable since these modifications will provide extended half life *in vivo*. It is taught that there are many modifications that are suitable for use in the oligonucleotides. It is taught that many linkage modifications such as phosphorothioate. It has been taught that 2' sugar modifications such as 2'-O-methyl and 2-O-alkyl are of interest in the facilitator oligonucleotides of their invention. Since the 2' modifications recited in the claims are all known 2' sugar modification known inn the art for oligonucleotide therapeutics and since Goodchild et al have taught that 2' sugar modifications are desirable in their invention it would be obvious to use any known 2' sugar modification that is known in the art to provide *in vivo* benefits, for example. Since, for example, Goodchild has taught that at least 20% or at least 50% modification is preferable but also includes oligonucleotides with one modification, the limitations of such as in claims 140 and 141 are met. One in the art would recognize that a 20mer with one modification would comprise "five to nine" 2'-hydroxyyl pentofuranosyl sugar moieties. The disclosure of Goodchild does not specifically teach a step of contacting their oligonucleotides with a double stranded nuclease, but since the teachings of Goodchild point to using their facilitator oligonucleotides in vivo it is reasonable to say that they will be used in human cells or in humans as therapeutics. Applicant invention is also drawn to the eventual use of the methods to treat human disease. The examiner can not make a determination of whether the oligonucleotides taught by Goodchild would in fact elicite a double stranded RNase cleavage since the Office is not equipped to make such a determination, however the prior art teaches compounds that meet the

structural requirements of the instant invention and further will be used in the same context[in human cells, for example] the Burden has been properly shifted to applicant to show that the prior art oligonucleotide would not have the same properties required of the compounds of the instant methods.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time of invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 99-104 and 143-145 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Each of claims 99-103 recite a phrase/limitation "the terminal . . . nucleosides" there is insufficient antecedent basis for this limitation in each of the claims. An oligonucleotide has at least 1 3' terminus and at least one 5' terminus. the context of the claims does not provide a context such that one in the art would know what terminus is referred to, for example. Claims 143-145 are rejected in so far as they depend on the claims above. claim 145 is further rejected since it recites "said each internucleoside linkage" there is insufficient antecedent basis for this limitation in the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43, 44, 94-104, and 135-189 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claimed invention is drawn to methods of cleaving a target RNA or activating a dsRNase via contacting a double stranded RNAase with specified oligomeric compound or contacting a specified oligomeric compound with a dsRNase.

The specification discloses rat liver extracts [T24 cells]with ds RNase activity. The specification does not provide a description of what this proteins structure is but provides only a method of isolating it. The specification also provides that an RNaser IV cleaved a particular dsRNA substrate and a showed that bacterial dsRNase did *not* cleave the substrate. The specification has therefore shown only one known structure for an RNAse that cleaves a ds substrate as claimed. The claimed methods are directed to encompass the use of corresponding "double stranded RNase" sequences from other species. None of these claimed methods meet the written description provision of 35

USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. Subsequent art [US 6,737,512, for example], shows that the subsequnnt isolation of human RNase III shows that it has 41% identity with *C.elegans,* 15-17% identity with yeast and, 16% homology with E.coli RNase III. It is taught in this subsequent art that the human RNase III is substantially larger and comprises more domains than the above RNase III's. The claimed invention requires the use of a vast range of ds RNasees where subsequent work has shown that the description provided in the instant specification is inadequate to practice the invention as broadly claimed. Applicants specification and the prior art describe but a few dsRNAses and the subsequent art has shown how diverse the encompases dsRNases are.

The instant specification therefore fails to provide any particular structure of dsRNases such that one in the art would know what dsRNases might function in the instant invention. At best one in the art is left with an assay to find other dsRNases that may function in the claimed methods.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc.,

that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent.

Accordingly, the specification does not provide a written description of the invention of claim 5.

The species specifically disclosed are not representative of the genus because the genus is highly variant as shown by the subsequent art, for example.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to /Sean R. McGarry/ whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean R McGarry/
Primary Examiner
Art Unit 1635

Notice of References Cited	Application/Control No. 10/281,349	Applicant(s)/Patent Under Reexamination CROOKE, STANLEY T.	
	Examiner /Sean R. McGarry/	Art Unit 1635	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-6,087,484	07-2000	Goodchild, John	536/23.1
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

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	N					
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	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
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	V	
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	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
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